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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

CHIN, C

ART UNIT

PAPER NUMBER

1641

DATE MAILED:

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15

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

08/081393

Applicant(s)

Fodstad et al

Examiner

C. Chin

Group Art Unit

1641

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

## Status

- ☒ Responsive to communication(s) filed on 11/16/99
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- ☒ Claim(s) 17-43 is/are pending in the application.
- Of the above claim(s) 34-37, 39, 40 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 17-33, 38, 41-43 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☒ Claim(s) 17-43 are subject to restriction or election requirement.

## Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been received.
  - ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
  - ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

\*Certified copies not received: \_\_\_\_\_

## Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 12
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other \_\_\_\_\_

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## **DETAILED ACTION**

### ***Claim Rejections - 35 U.S.C. § 103***

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 17-33 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al in view of Connelly for the reasons of record in paper 10.

In response to this rejection, Applicants present the following arguments:

a.) Applicants argue that Widder et al (herein referred to as Widder) fail to teach detection of individual target cells as claimed in the present invention. Widder discloses a method for coarse separation of blood cells and not detection of individual target cells.

Applicant's argument has been considered but is not convincing. Widder teaches a method for separation of a select population of cells, bacteria, or viruses from a mixed population thereof, in which microspheres containing magnetic particles are coated with a layer of antibodies which selectively bind to the select population of the mixed population of cells, bacteria, or viruses (page 4). The microspheres are also labeled with a fluorescent label as shown in Example I which teaches preparation of the microspheres. Contrary to Applicant's argument, Widder teaches the detection of a population of target cells from a mixed population of cells as in the instant invention. The antibodies on the microspheres provide for highly specific binding to the target

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cells (or bacteria or virus) which separates them from the rest of the mixed population.

Furthermore, the use of fluorescent labels on the microspheres provides for detection of the target cells as well as for quantitation of the target cells. The method of Widder is not limited to the separation of blood cells as argued by Applicants. While the examples may show using the method of Widder for separation of blood cells, it is improper to say that the method of Widder is limited to just the separation of blood cells.

b.) Applicants argue that the use of protein A on the microspheres of Widder will cause the microspheres to adhere to non-target cells and target cells alike which results in an unacceptable reduction in specificity. In addition to binding the Fc portion of IgG, protein A will also bind to B cells and plasma cells present in a sample.

Applicant's argument has been considered but is not convincing. While Applicants assert that the use of protein A by Widder would result in an unacceptable reduction in specificity, Applicants have not provided any experimental evidence to support their assertions. A side-by-side comparison would be required to support any assertion that the method of Widder is any less sensitive than the instantly claimed method.

c.) Applicants argue that the method of Widder cannot achieve the sensitivity required by the present invention. Applicants assert that the content of iron in Widder's microspheres varies. The magnetic strength of the microspheres is not powerful enough to pull a few target cells out of a population of several million cells.

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Applicant's arguments have been considered but are not convincing. While Applicants assert that the method of Widder cannot achieve the level of sensitivity required by the instant invention, Applicants have not provided any experimental evidence to support their assertions. Applicants also have not provided any evidence to show that the iron content in the microspheres of Widder do in fact vary or that the magnetic strength of Widder's microspheres is not powerful enough to pull out the target cells.

d.) Applicants argue that the method of Widder involves non-specific binding reactions which is unacceptable.

Applicant's argument has been considered but is not convincing. The method of Widder employs antibodies on the microspheres which are highly specific for the target cells. Thus, the method of Widder does not involve non-specific binding reactions.

e.) Applicants argue that the concept of using the particle-target-cell complex to visually detect the cells with a microscope has not been accomplished previously, since it has not been possible to obtain particle binding exclusively to target cells. Applicants refer to criticism from colleagues at the Norwegian Radium Hospital that the present invention would suffer from the same disadvantages as encountered in Widder.

Applicant's arguments have been considered but are not convincing. The method of Widder shows that it is possible to obtain particle binding exclusively to target cells. Widder's use of antibodies on the particles (microspheres) makes it possible to target specific cells in view of the high specific binding affinity of the antibodies to the target cells. The criticism from colleagues

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at the Norwegian Radium Hospital offer no probative value as they amount to nothing more than here say. There is no declaration showing that these colleagues made such criticism nor is there any experimental evidence to support their criticism.

f.) With respect to Connelly, Applicants argue that the fixative used in Connelly results in killed cells.

Applicant's argument has been considered but is not convincing. The instant claims fail to recite any limitations that require the cells to be alive. Applicant's argument is directed to a limitation that is not being claimed.

g.) Applicants also argue that the use of detergents "does not necessarily increase the specificity of the method" but then go on to say that "use of a combination of detergents at [and] low concentration and low temperatures surprisingly gave the specificity of the presently claimed method".

First, Applicants arguments are contradictory as it is not clear as to whether Applicants are saying that the use of detergents, or lack thereof, increases the sensitivity of the instant method. Second, the optimum temperature and concentration of detergent that is to be employed can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art.

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3. Claims 17-33, 38, and 41-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al in view of Kemmer et al and Terasaki et al for the reasons of record in paper 10.

In response to this rejection, it is noted that Applicants have directed specific arguments to the Kemmer et al and Terasaki et al references without considering the combination of references. Such arguments are improper as Kemmer et al and Terasaki et al were not applied as 102 anticipatory references.

#### ***Conclusion***

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chris Chin whose telephone number is (703) 308-3991. The examiner can normally be reached on Monday-Thursday from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

cchin/cc  
February 9, 2000



CHRISTOPHER L. CHIN  
PRIMARY EXAMINER  
GROUP 1800-1691